UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,900	10/18/2001	Masomeh B. Sticklen	MSU 4.1-539	9143

21036 7590 02/18/2004

MCLEOD & MOYNE, P.C.
2190 COMMONS PARKWAY
OKEMOS, MI 48864

EXAMINER	
KALLIS, RUSSELL	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,900	STICKLEN ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-104* is/are pending in the application.

4a) Of the above claim(s) *18-46,83-99,101 and 104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,47-82,100,102 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/18/2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/18/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-104 are pending. Claims 18-46, 83-99, 101 and 104 are withdrawn and Claims 1-17, 47-82, 100, 102 and 103 are examined.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-17, 47-82, 100, 102 and 103 in Paper No. 10/30/2003 is acknowledged. The traversal is on the ground(s) that Applicant would have to file separate applications on each of the related sequences. This is not found persuasive because as stated in the previous office action the separate inventions of Groups I, II, and III are unrelated and the nucleotide sequences have either different structure or function and would require additional searches that would be a burden to the office.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

New corrected drawings are required in this application because the hand drafted drawings are not clearly drafted are too light or weak in tone to provide for legible copying. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 47-82, 100, 102 and 103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims any plant transformed with any polynucleotide encoding a cellulase (i.e. anyone of a wide variety of enzymes that degrade cellulose) and any ligninase (anyone of a wide variety of enzymes that degrade lignin) and a method of producing a plant that degrades lignocellulose comprising any cellulase and any ligninase.

Applicant describes a cellulase of SEQ ID NO: 4 (*e1*), SEQ ID NO: 6 (*cbh1*), SEQ ID NO: 8 (a dextranase), and SEQ ID NO: 10 (a beta-glucosidase); and ligninases of SEQ ID NO: 11 (*ckg4*) and SEQ ID NO: 13 (*ckg5*) all of microbial origin.

Applicant does not describe the polynucleotides encoding the various categories of enzymes that would degrade lignocelluloase other than SEQ ID NO: 4, 6, 8, and 10; and SEQ ID NO: 11 and 13.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of

cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a ligninase or a cellulase falling within the scope of the claimed genus of polynucleotides which encode enzymes that degrade lignin or cellulose. Applicants only describe a cellulase of SEQ ID NO: 4 (*e1*), SEQ ID NO: 6 (*cbh1*), SEQ ID NO: 8 (a dextranase), and SEQ ID NO: 10 (a beta-glucosidase); and a ligninase of SEQ ID NO: 11 (*ckg4*) and SEQ ID NO: 13 (*ckg5*) all of microbial origin. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for ligninase or cellulase protein activity, it remains unclear what features identify a ligninase or cellulase encoding polynucleotide. Since the genus of ligninase or cellulase encoding polynucleotides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Claims 1-17, 42-82, 100, 102 and 103 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transformed herbaceous plant comprising a DNA encoding a cellulase and a lignase operably linked to a plastid targeting DNA, does not reasonably provide enablement for a woody plant so transformed or for a transformed plant comprising a DNA encoding a cellulase and a ligninase operably linked to a DNA for targeting to any organelle. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims a transgenic plant comprising a DNA encoding a cellulase and a ligninase targeted for expression to an organelle and which degrades lignocellulose when the transgenic plant is ground and a method thereof.

Applicant teaches heterologous DNA expression cassettes comprising the signal sequence from *rbcs* for targeting proteins to the chloroplast and isolated polynucleotide sequences encoding a cellulase of SEQ ID NO: 4 from *Acidothermus cellulyticus* (E1, a cellulase), SEQ ID NO: 6 from *Actinomyces naewslundi* (a beta-glucosidase), SEQ ID NO: 8 from *Streptococcus salivarius* (a dextranase), or SEQ ID NO: 10 from *Trichoderma reesei* (*cbh1*); and a ligninase of SEQ ID NO: 4 (*ckg4*) or SEQ ID NO 11 (*ckg5*), from *Phanerochaete chrysosporium*, all known in the art (Examples 1-4); and provides prophetic guidance for a method of transformation of maize with said heterologous DNA constructs and plants thereof

(Examples 5-6) and analysis of ground transformed maize tissue for cellulase and ligninase activity (Examples 7-9).

Applicant does not teach transformation of any plant or provide guidance for transformation of any plant by targeting expression to any organelle of any cellulase and any ligninase other than the guidance provided for in the specification for the transformation of maize using the cellulases of SEQ ID NO: 4, 6, 8, and 10, and the ligninase of SEQ ID NO: 11 and 13 targeted to the chloroplast using *rbcs* signal peptide. Further, Applicant does not teach methods of transforming and expressing or analyzing the activity of cellulase and ligninase in woody plants or a woody plant transformed thereof.

The problematic nature of recovering transgenic plants expressing proteins targeted to the ER that are by their nature damaging to the plant is made evident in the transformation of alfalfa with a lignin degrading peroxidase enzyme Mn-P. Researchers observed severe senescence in trifoliates several weeks after transformation that resulted in death of the plant or the inability to recover enough clonal copies for adequate field studies in transformed alfalfa plants expressing moderate to high levels of Mn-P. Further, (Austin S. *et al.* Euphytica, 1995; Vol. 85 pages 381-393; page 386 column 2; and page 388 see field performance).

Further, any woody plant species would present a significant challenge given that the amount of woody material, devoid of organelles, out weighs the herbaceous part of the plant where the celllulase and ligninase are expressed, such that there is not enough cellulase and ligninase to degrade so great a mass of lignocellulose. This is made even more problematic as an experimental task when considering that most woody tissues are not easily ground and often contain resins and phenolics that render enzymes inactive, and hence the cellulase and ligninase

expressed in the herbaceous part of the plant would be unable to reach those tissues to effectively degrade the lignocellulose.

although one of skill in the art can readily make transformed plants one would not know based upon Applicant's disclosure which embodiments would be operable and thus undue trial and error experimentation would be needed by one skilled in the art to make and clone a multitude of non-exemplified cellulase and ligninase encoding DNA sequences and would require one of skill in the art to test in a myriad of non-exemplified plants for lignocellulose degradation in a multitude of non-exemplified transformed plant species.

Given the unpredictability in the art as to which organelle would tolerate the presence of active cellulase and ligninase and also protect the transformed plant from damage and where to target cellulase and ligninase activity in a large woody plant; the breadth of the claims encompassing any plant transformed with any cellulase and any ligninase; the lack of guidance in the examples of the specification or in the prior art as to which cellulase and ligninase in which organelle would best degrade lignocellulose in a transformed plant, woody or otherwise; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17, 47-82, 100, 102 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Himmel M. *et al.* U.S. Patent 6,013,860 issued January 11, 2000, in view of Crawford *et al.*, U.S. Patent 5,200,338 issued April 6, 1993; and in further view of de Boer, H. *et al.* Gene, 1987, Vol. 60; pages 93-102 and Applicants addmissions.

Applicant broadly claims a transgenic plant comprising a DNA encoding a cellulase and a ligninase targeted for expression to an organelle and which degrades lignocellulose when the transgenic plant is ground and a method thereof.

Himmel teaches methods of engineering of plants to reduce the content of cellulose into fermenatables in a plant by expressing lignocellulose degrading enzymes (i.e. a cellulase enzyme) in the plastid (column 1, line 61 to column 2, line 63) and plants thereof; tobacco transformation in column 9, and incorporates through reference U.S. Patent 5,536,655 that teaches SEQ ID NO: 4 (column 4, lines 16-36); an alternative method for expression of the cellulase in a plastid by nuclear transformation and targeted expression to the plastid wherein the cellulase encoding DNA is operably linked to a DNA encoding a plastid targeting sequence (in column 4, lines 45-56; and as taught in Applicant's specification on page 23 as GenBank Accession number X07515 (i.e. SEQ ID NO: 1) first made available to the public in Kyozuka J. *et al.*, Plant Physiol., 1993; Vol. 102 (3), pages 991-1000); and degradation of lignocellulose after grinding (see column 11); a *rbcS* leaf specific promoter, a DNA encoding a chloroplast transit peptide, and an antibiotic selectable marker operably linked to a constituitive promoter, incorporated through reference to U.S. Patent 5,576,198 McBride K. *et al.* see Columns 5 and 4 and figure 1.

Himmel does not teach a ligninase or sexual fertilization of two transformed plants producing a third transgenic plant comprising a heterologous ligninase and cellulase.

Crawford teaches the necessity of removing lignin from lignocellulose in order to degrade cellulose (column 1, lines 38-54) and the identification of polynucleotides encoding ligninases from *Phanerochaete chrysosporium* incorporated through reference (column 2, lines 41-44; Zhang *et al.* Biochemical and Biophysical Research Communications; 1986, Vol. 137: pages 649-656).

De Boer teaches CLG4 i.e. SEQ ID NO: 11 also known as H2 and *ckg4* (specification page 25, lines 24-30; see attached sequence report). Further, Applicant admits that methods for converting lignocellulose in a plant material to fermentable sugars were known in the art on pages 3-4 of the specification; incorporates through reference SEQ ID NO: 1 as GenBank accession number X07515 on page 23 of the specification; and teaches on page 37 of the specification that the *bar* gene from *Sterptomyces* encoding phophinothricin acetyltransferase is well known in the art.

It would have been obvious at the time of invention to modify the invention of Himmel to include a ligninase. One of skill in the art would have been motivated by the knowledge common in the art that ligninase gene products are valuable materials for breaking down lignocellulose into fermentables as taught by Crawford and Himmel and that ligninase genes and promoters and DNA encoding transit peptides were available in the art as taught by de Boer and Applicant's specification, that one would have had a reasonable expectation of success of selecting transformed plants using *bar* and of expressing genes in transformed plants and plant cells; and

wherein sexual fertilization as a method of combining two transgenes into one plants is an obvious design step given the lack of criticality.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
February 2, 2004

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600